EXHIBIT E

Translation of submission of Maiwald GmbH Patent Attorneys to German Patent Office of 9 February 1999
P 44 47 287.0-41
IDEA Innovative Dermale Applikationen GmbH

Opponent: ROVI GmbH

In response to the German Patent Office's Communication of 8 April 1998, and the response of the Opponent of 17 March 1998 submitted therewith:

It is politely requested to issue a Communication of the Opposition Division of the German Patent Office in advance, before it is decided in this Opposition matter, which is of extreme importance for our client.

I. Admissibility

According to § 59 I German Patent Law, in an opposition procedure, the opposition grounds have to be substantiated, in order to make the opposition admissible, i.e. it is necessary that the facts, whereupon the opposition is based, have been provided within the opposition period. In other words, the Opponent has to go into each feature of the claims, in that the Opponent has to provide the page and the line of the prior art document, wherein this feature allegedly is anticipated.

However, this is what the Opponent has failed to do, namely to go into the details of the features of the main claims 1 and 22, as well as into the dependent claims of the patent in detail, in a substantiated manner. It would have been easy for the Opponent to list every feature of the independent and dependent claims, where and at which position substantiated statements have been provided in the letter of opposition, which has been submitted within the opposition period. Instead of doing so, the Opponent tries to make up for the missed action by lengthy lyric and belated statements.

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Only indicating a document, as the Opponent did, is not in conformity with the demands as to admissibility according to § 59 I German Patent Law.

It has to be emphasized that the requirements for admissibility have to be fulfilled within the opposition period, and that an opposition which is once inadmissible, cannot be made admissible, in that one provides the missed statements after expiry of the opposition period.

II. The Opponent states that the patent does not disclose the invention in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

An invention is disclosed sufficiently clear and complete, if an ordinary, skilled person recognizes the kind of the technical teaching by reading the description and by logical interpretation thereof, and is thus able to carry out the teaching accordingly. Some experiments to a limited extent are not too much to be expected of a person skilled in the art.

Lack of clarity of the patent claims is, however, no opposition ground. An opposition cannot be based thereupon, only.

The Opponent tries to convey that the subject matter claimed by the patent is not feasible, supported by pure assertions. Thus, the Opponent argues by way of example that the term "permeation capability" is unclear for a skilled person in its technical meaning.

This has to be opposed. The term "permeability" is derived from the Latin word permeare = going through something, migrating, passing something. The term "permeability" designates the porosity of optionally porous barriers for agents. From permeation, the skilled person understands the procedure of migrating or seeping of an agent through another one.

Furthermore, on pages 10-13 of the description of the granted patent, detailed statements concerning the determination of the carrier/permeation capability are provided. In particular, Table 2 lists the pore diameter, the pressure and the permeation capability obtained for each sample. Additionally, a series of examples is disclosed, which the skilled person simply has to rework.

It is thus not understandable, how the Opponent comes to the conclusion that the subject matter of the patent is not sufficiently disclosed, without having made the effort, at least once, to rework at least one of the disclosed examples.

In summary, it has to be pointed out that the statements of the Opponent that certain formulations of the patent should be either not understandable, or not clear, are no opposition ground according to § 21. The argumentation provided now, after expiry of the opposition period, that that the claimed subject matter according to the patent is not sufficiently disclosed, is thus, as mentioned above, unfounded.

III. Discussion of prior art

There is no indication whatsoever in D1 that the preparation comprises at least two components differing in their solubility in the suspension medium of the preparation, normally water, by a factor of at least 10, and the amount of solubilizing components is less than 0.1 mol %, referring to the amount of these substances at which the point of solubilization of the covered droplets is reached or this point of solubilization cannot be reached. Thus, the claimed subject matter according to the patent is novel over D1.

As already detailed in our submission of 11 July 1997, D1 discloses preparations, which comprise an amount of a surface-active substance, which corresponds up to 99 mol % of the amount of this substance, by which the point of solubilization of the droplets is reached. In

contrast to the present invention, the amount of surface-active substance is, in full awareness, selected in such a way that one approaches the point of solubilization, which is the amount at which the droplet would dissolve. Thus, an optimisation of the penetration capability is done by calculated stress of the stability parameters. As a result, preparations for the transport of active agents are obtained according to D1, which are optimised in their penetration capabilities by adjusting the amount of a surface-active substance near the point of solubilization.

The present invention is totally different. Here, the preparations with an amount of solubilizing components of less than 0.1 mol % according to claim 1 show a high mechanical elasticity and deformability under stress, although the skilled person would not expect this, due to the high stability which would have to be expected, instead. In other words, the claimed preparations according to the invention are able to penetrate through permeation barriers, like skin, although they have a small amount of solubilizing components (i.e. far off from the point of solubilization and not near to it).

Consequently, D1 is no relevant prior art, since it discloses an opposite teaching, compared to the present invention, namely to optimize the penetration capability of preparations by working with an amount of up to 99 mol % of solubilizing components near the point of solubilization.

Document D2 discloses on page 42, Fig. 5, a ternary phase diagram of any mixture of lecithin/lysolecithin/water at 52°C.

According to the patent, systems are claimed which are suitable for transportation of active agents through skin. Skin temperature is normally at about 32°C, and especially the outer skin layers have a much lower temperature. Consequently, the ternary phase diagram at 52°C disclosed in D2 is not transferable to the inventive system.

Document D3 discloses no preparations for the application or the transport of at least one active agent ~~in two~~ into and through barriers and constrictions, like skins. It has to be emphasized that between the claimed preparations according to the patent and those liposomes disclosed in D3, a fundamental technical difference exists. The claimed preparations according to the patent can transport active agents through the skin, whereupon the active-agent-containing preparations get through the barrier, without destruction of the membrane-like sleeve.

The liposomes according to D3 behave totally differently. Liposomes described in D3 function as depot-drug-carriers, i.e. the liposomes slowly release the active agent. The active agent, thus released, enters the skin free of liposomes.

Consequently, D3 is not relevant as prior art, as already pointed out in detail in our previous submission. Finally, D3 does not contain any indication that the components should differ in their solubility in the suspension medium of the preparations by a factor of at least 10, and that the amount of solubilizing component should be less than 0.1 mol %, referring to the amount of this substance at which the point of solubilization of the covered droplets is reached, or instead, the point of solubilization cannot be reached.

D4 and D5 do not concern any preparations for the transport of agents into and through natural barriers and constrictions like skins and the like. Thus, D4 and D5 do not belong to the same technical field as the granted patent, and are thus not relevant.

Since none of the prior art documents, neither alone nor in any combination, anticipates or suggests the subject matter of claim 1, also the method claim 22, comprising the features of claim 1, is based on a novel and inventive teaching.

Thus, the Opposition has to be rejected as inadmissible and/or unfounded.

Signed by Dr. Stefan Michalski